Citation:

Rimm EB, Williams P, Fosher K, Criqui M, Stampher MJ. Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. *BMJ.* 1999; 319: 1523-1528.

PubMed ID: 10591709

Study Design:

Meta-analysis or Systematic Review

Class:

M - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To quantitatively summarize the effects of moderate alcohol intake on biomarkers of risk of coronary heart disease (CHD) and to determine the projected impact of those changes on risk of CHD.

Inclusion Criteria:

- MEDLINE search for all experimental studies of alcohol in humans published in English between 1965 and 1998. Medline search was supplemented with citations from review articles, meeting and symposia proceedings and the *Journal of the Alcohol Beverage Medical Research Foundation* and *Alcohol Research.* The search was restricted to the following:
  - Studies in individuals without diagnosed CHD, diabetes or alcohol dependence
  - Studies that assessed biomarkers consistently modified by alcohol and related to risk of coronary heart disease
  - Studies with an intervention period of at least seven days when examining lipid factors
  - All studies of coagulation and thrombolytic factors regardless of intervention period
- Only studies that included the following information were included in the final analysis:
  - Number of participants
  - Age range of participants
  - Participant sex
  - Average dose of alcohol
  - Study duration
  - Beverage type
  - Change in a biomarker compared with its pretreatment measurement or compared to a comparable group of placebo or untreated participants.

Exclusion Criteria:

- Studies in which participants consumed 100g or more of ethanol per day
- Studies of lipid peroxidation and platelet aggregation.

Description of Study Protocol:

Recruitment

- MEDLINE search for all experimental studies of alcohol in humans published in English between 1965 and 1998
- MEDLINE search was supplemented with citations from review articles, meeting and symposia proceedings, and the *Journal of the Alcohol Beverage Medical Research Foundation* and *Alcohol Research.*

Design

- Weighted linear regression: Each biological measure was fitted a zero intercept weighted linear regression model predicting change in the biological marker for alcohol intake as a continuous variable:
  - Each study was weighted by the inverse of the variance of the change measure
  - If no variance measure was provided, the average weight from the remaining studies was used for weighting
  - For biomakers with less than 10 data records, regression were weighted by the size of the study
- Weighted least squares linear regression:
  - Mixed effects model structure used
  - Study was treated as a random effect
  - Biomarkers were used as dependent variables
  - Dose of alcohol, sex, age, beverage type and study duration were treated as fixed effects
- Predicted mean change in each biomarker after an intake of 30g alcohol per day was calculated
- Previously published studies linking a change in each biomarker to risk of CHD were used to calculate the predicted relative risk (RR) of CHD that would be expected on the basis of the change in each biomarker achieved by consuming two drinks per day.

Statistical Analysis

- Weighted linear regression
- Weighted least squares liner regression with study treated as a random effect.

Data Collection Summary:

Timing of Measurements

Studies published between 1965 and 1998.

Dependent Variables

- High-density lipoprotein (HDL)
- Apolipoprotein A I

- Triglycerides (TG)
- Plasminogen
- Fibrinogen
- Lp(a) lipoprotein
- Tissue type plasminogen activator antigen
- von Willebrand factor.

Independent Variables

- Dose of alcohol
- Sex
- Age
- Beverage type (beer, wine, spirits or ethanol)
- Study duration.

Description of Actual Data Sample:

- *Attrition (final N):* 42 experimental studies, providing 67 separate data records. Six of these records were excluded from the main analysis.
- *Age:* 18 to 65 years
- *Other relevant demographics:*
  - Studies used included both men and women
  - Studies of alcohol intake and changes in HDL and apolipoprotein A I ranged from from one week to three months in duration
  - Studies of alcohol intake and biochemical measures of thombolysis and coagulation range from one day to six weeks in duration.

Summary of Results:

Variables	HDL	Apolipoprotein A I	TG	Fibrinogen	Plasminogen Activator Antigen	Lp(a) Lipoprotein
Number of data records included	36 records from 25 studies	24 records from 24 studies	35 records	No data	No data	Five data records from four studies
Average alcohol consumption (g per day)	40.9	37.6	No data	No data	No data	No data
Average study duration	4.1 weeks	3.9 weeks	No data	No data	No data	No data
Change in biomarker concentration	5.1mg per dL	11.83mg per dL	No Data	No data	No data	No data

Change in biomarker concentration per gram alcohol consumed per day (weighted)	0.133mg per dL	0.294mg per dL	0.19mg per dL	No data	No data	No data
Change in biomarker concentration expected if consuming 30g alcohol per day compared to abstaining (95% CI) (mg per dL)	3.99 (3.25 to 4.73), P<0.05	8.82 (7.79 to 9.86), P<0.05	5.69 (2.49 to 8.89), P<0.05	-7.5 (-17.7 to 32.7)	1.25 (-0.31 to 2.81)	-0.7 (-3.38 to 1.99)

Consuming 30g of alcohol daily is significantly associated with an increase in HDL, apoliporotein A I, plasminogen (1.47%; 95% CI: -1.18% to 4.42%; P<0.05) and TG concentrations, but not associated with a change in fibrinogen, Lp(a) lipoprotein or tissue type plasminogen activator agent concentrations.

Projected Percentage Reduction in Risk of Coronary Heart Disease Attributed to Effects of Alcohol on Concentrations of High Density Lipoprotein Cholesterol, Fibrinogen and Triglycerides

		Projected Reduction in Coronary Heart Disease Associated with 30g Alcohol per Day vs. Abstaining (Percent)	
Biomarker	**Relative Risk (95% CI) from Published Study**	**Unadjusted**	**Adjusted for Intra-individual Variability**
High density lipoprotein cholesterol	0.69 (0.47 to 0.99) per 10mg per dL[32]	13.5	16.8
Fibrinogen	1.34 (1.15 to 1.56) per 50mg per dL[29]	4.3	12.5
Triglycerides	1.40 (1.10 to 1.77) per 100mg per dL[33]	-19	-4.6
Total		15.9	24.7

Based on the results of this meta-analysis, the change in the concentrations of HDL, fibrinogen and TG associated with an alcohol intake of 30g per day is expected to reduce risk of coronary heart disease by 24.7%.

Other Findings

For HDL:

- Among five studies with average baseline HDL concentrations less than 40mg per dL, the effect of alcohol was stronger (B=0.138mg per dL) than among the 18 studies with concentrations higher than 48mg per dL (B=0.110, P=0.04).

Author Conclusion:

Results suggest that moderate alcohol intake is causally related to lower risk of CHD through alcohol-induced changes in lipids and hemostatic factors.

Reviewer Comments:

- *The interpretation of modification effects is not presented clearly. For example, "Among men (29 records) the coefficient for a 1g increase in alcohol was stronger (B=0.134mg per dL) than in women (three records) (B=0.095mg per dL; interaction, P=0.93)," The authors seem to be noting a difference between coefficients despite a non-significant interaction. For this reason, the results regarding effect modifications were not included. Additionally, these results are not the primary analysis.*
- *A table of the studies included in the meta-analysis is available on-line from the BMJ with the full-text article. This abstractor included these tables when completing the Research Design and Implementation Rating Checklist and when considering the overall rating for this paper.*
- *The authors did not explicitly state the search terms used in their description of the study methods or the number of abstracts reviewed. However, the general search terms can be inferred from the Methods discussion.*
- *The authors do not discuss the distribution of the effect sizes of the studies included in the analysis. In addition, the variance associated with the effects observed from the studies included is not presented.*
- *The authors do not include the standard errors of the beta-coefficients presented in the results.*

Research Design and Implementation Criteria Checklist: Review Articles

Relevance Questions		
1.	Will the answer if true, have a direct bearing on the health of patients?	Yes
2.	Is the outcome or topic something that patients/clients/population groups would care about?	Yes
3.	Is the problem addressed in the review one that is relevant to nutrition or dietetics practice?	Yes

4.	Will the information, if true, require a change in practice?	Yes

Validity Questions

1.	Was the question for the review clearly focused and appropriate?	Yes
2.	Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search termsused described?	Yes
3.	Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased?	Yes
4.	Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible?	Yes
5.	Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined?	Yes
6.	Was the outcome of interest clearly indicated? Were other potential harms and benefits considered?	Yes
7.	Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described?	???
8.	Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed?	Yes
10.	Was bias due to the review's funding or sponsorship unlikely?	Yes